## REMARKS

Applicant respectfully requests reconsideration. Claims 76-78, 81, 86-88, 91, 108, 110, 112, 115-120 and 124-177 were previously pending in this application. No claims are amended herein. As a result, claims 76-78, 81, 86-88, 91, 108, 110, 112, 115-120 and 124-177 are still pending for examination with claims 76, 78, 81, 86, 88, 91, 110, 112, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170 and 174 being independent claims. No new matter has been added.

## Rejection Under 35 U.S.C. 103

Claims 76-78, 81, 86-88, 91, 108, 110, 112, 115-120 and 124-177 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Crooke et al. (US Patent 6,107,094), as evidenced by Tuschl et al. (US 20040259247 A1) and Amarzguioui et al. (2003) *Nucleic Acids Res.* 31:589-595.

The Examiner characterizes Crooke et al. as teaching "double stranded RNAs of 17 and 20 base-pairs in length for purifying and characterizing mammalian dsRNAses." The Examiner further states that "[I]t is said that the oligoribonucleotide gapmers, and i.e., impliedly, dsRNAase substrates comprising said gapmers, (i.e. dsRNAs) may be from about 5 to about 50 nucleotides in length, or more preferably, from about 15 to about 25 nucleoside subunits in length (col. 14 lines 10-20)." (Office Communication pages 7-8). It is further stated that "[I]t is implied that various dsRNAs of various lengths in the recommended range (15-25 and 5-50) and with various flanking chemical modifications could be used in such an assay for characterizing dsRNAse activity from almost any mammalian cell type". (Office Communication page 8). According to the Examiner, on the basis of the disclosure of Crooke et al. one of skill in the art "would have immediately envisioned chemically and non-chemically modified dsRNAs of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, and 25 nucleotides in length complementary to a mammalian gene."

According to the Examiner one of skill in the art would have had reason to synthesize and use such dsRNase substrates because of "the normal desire of the scientist to explore, expand upon, and understand the activities of mammalian dsRNases as taught by Crooke et al." (Office Communication, page 9).

The Examiner relies on Tuschl et al. (US 20040259247) and Amarzguioui et al. (2003. Nucleic Acids Res. 31:589-595) for "showing that a property is inherent." The examiner states that "there is sufficient reason to believe the dsRNase substrates of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, and 25 nucleotides in length and longer up to and including 50 nucleotides in length, taught by Crooke et al. would mediate RNAi of the gene to which they are targeted." This rejection is respectfully traversed.

**The Pending Claims Are Not Obvious In View of Crooke**

It is Applicants' position that the Examiner has failed to make a proper prima facie obviousness rejection. In particular, as set forth in detail below, it is Applicants position that the Examiner has used impermissible hindsight, having Applicants' specification in hand, to (i) apply the teachings of Crooke with respect to length ranges suitable for *single-stranded oligonucleotides* (e.g., 5-50 or 10-25 nucleotide in length), to arrive at molecules which the Examiner contends are "implicitly" taught, i.e., dsRNAs with a length range of 5-50 or 10-25 nucleotides; and (ii) extract a specific size range from within these broader ranges to arrive at the claimed invention.

The claims pending in the instant application are directed to isolated double stranded RNA of from 21 to 23 nucleotides, having complementarity to a mammalian cellular mRNA to mediate RNAi by directing cleavage of the mRNA within the region of complementarity.

Crooke teaches a class of complementary oligomeric compounds for use in inhibiting cellular targets (commonly called antisense compounds). The antisense compounds of Crooke differ from classical, DNA-based oligos in that they purportedly hybridize to target mRNA and mediated double-stranded RNAse (dsRNAse) cleavage of the oligo:mRNA hybrid whereas classical, DNA-based antisense oligos hybridize to target and mediate RNAaseH cleavage of the mRNA target. To facilitate this activity, Crooke teaches single-stranded RNA-like oligomeric compounds having subsequences of ribofuranosyl (e.g., 2'-pentofuranosyl) nucleosides that activate dsRNAse. The oligomeric compounds contain modifications (e.g., 2'-substituent group, nucleobase and/or internucleoside linkage modifications) that increase pharmacokinetic properties (e.g., affinity for mRNA) and/or nuclease resistance. Crooke further teaches dsRNAses identified in cultured

(e.g., T24 cells) and liver homogenates, as well as specific artificial substrates designed to characterize the activities of such RNAses.

A proper *prima facie* obviousness rejection requires that the Examiner set forth a clear articulation of the reason(s) why the claimed invention would have been obvious in view of the prior art and provide an explicit analysis to support the rejection, without the use of hindsight based on applicant's disclosure. See MPEP 2141(III). Applicants respectfully submit that the Examiner has not met this burden.

The Only Isolated RNA Duplexes Disclosed By Crooke Are 17 and 20 Nucleotides In Length

The disclosure of Crooke is primarily directed to antisense molecules which, in contrast to the molecules of the pending claims, are ***single-stranded*** oligomeric molecules which "have certain RNA like features that allow them to form a double stranded structure with a targeted RNA region and this double stranded structure is subsequently degraded by eukaryotic dsRNases." (paragraph spanning columns 9 and 10). These oligomeric molecules are referred to as "gapmers" by the reference. These single-stranded oligomeric compounds described and claimed in Crooke et al. would only form double stranded molecules with target RNAs under test conditions in a cell or test solution. The Crooke antisense molecules include about 5 to about 50, or about 15 to about 25, or about 8 to about 50 or about 12 to about 30 or at least 12 nucleoside subunits.

In addition to the featured gapmer antisense molecules of the Crooke disclosure, there is disclosure of one 17 nucleoside and three 20 nucleoside artificial substrates for mammalian RNAses which are double-stranded. In contrast to the gapmer antisense molecules of the disclosure, these double-stranded molecules are used as RNase substrates to partially purify newly identified RNases. The isolated RNA duplexes described by Crooke et al. are present in Table 1 in Example 27. No other dsRNA compounds are exemplified in Crooke et al.

Contrary to the Examiners assertion, the text relating to size limitations referenced in Crooke et al. actually refers to the antisense, single-stranded gapmers disclosed therein. With respect to these molecules, the reference discloses size ranges of from about eight to about fifty or from about twelve to about thirty linked nucleoside subunits (col 4, lines 29-38), compounds including at least

twelve nucleosides for use in methods (col. 7, lines 20-25) and discloses that preferred oligoribonucleotides and oligoribonucleosides comprise from about 5 to about 50 nucleoside subunits or from about 15 to about 25 nucleoside subunits (col. 14, lines 8-22). In each instance, the reference is teaching size ranges for the single-stranded antisense gapmers. Nowhere does the reference teach any size range for artificial substrates. Only artificial substrates of 17 and 20 nucleosides are described. One of skill in the art reading the Crooke disclosure would have understood that the size ranges of the disclosure do not apply to the double-stranded RNAse substrates described therein. The Examiner, having Applicants disclosure as a blueprint, has gone on a fishing expedition in the text of the Crooke reference and applied the teaching regarding size of antisense gapmers for mediating dsRNA cleavage of target mRNA to artificial dsRNAse substrates for characterizing newly identified dsRNAses. The abundant use of hindsight is evident by repeated reference to the "*implied*" or "*implicit*" teachings of the reference throughout the Office Action with a lack of any evidentiary support or rationale as to why such teachings are allegedly implicit. The skilled artisan reading Crooke would have understood the reference to merely teach artificial dsRNAse substrates as described in Example 27 and nothing more.

The Reference Provides No Motivation To Make Double Stranded Molecules Of Lengths Other Than 17 And 20 Nucleotides, Let Alone 21, 22, Or 23 Nucleotides In Length

The substrates that are described in the working Examples of Crooke are dsRNAs of 17 and 20 nucleotides in length. Crooke et al demonstrated that dsRNA of 17 and 20 nucleotides in length were sufficient for isolation and characterization studies of the dsRNase. The Examiner asserts that one of skill would have had reason to synthesize and use dsRNase substrates of 15-25 nucleotides in length because, "it would have been the normal desire of the scientist to explore, expand upon, and understand the activities of mammalian dsRNases as taught by Crooke et al. " Applicants respectfully disagree. The Crooke patent simply does not provide a motivation for the skilled artisan to synthesize and use dsRNA of lengths other than 17 or 20 nucleotides in length. A general desire to conduct research without some aim or guidance is not sufficient motivation. The only motivation to make dsRNA of 21-23 nucleotides in length comes from the disclosure of the instant

invention, where it is taught that dsRNA of such length has important functional properties (i.e., RNAi-mediating properties).

In KSR, the Supreme Court noted that key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. See MPEP 2141(III). Applicants submit that, "the normal desire of the scientist to explore, expand upon, and understand..." an activity is not one of the rationales set forth in KSR to support an obviousness rejection. Applicant respectfully submits that applying this open-ended rationale to support an obviousness rejection, without some indication that such desire (if it existed) would lead the scientist in the particular direction of the claimed invention, constitutes improper use of hindsight. Applicant submits that even if "the normal desire of the scientist to explore, expand upon, and understand..." an activity could in theory support an obviousness rejection, and even if Crooke impliedly taught dsRNA substrates of 5-50 or 15-25 nt in length, which Applicant does not concede, the Examiner has not explained why or how the use of short dsRNA of 21-23 nucleotides rather than the 17 or 20mers disclosed by Crooke would fulfill the alleged desire of the scientist to explore, expand upon, and understand the activities of mammalian dsRNases.

In Example 27, Crooke described development of a dsRNA substrate that could be used to assay dsRNAase activity for purposes of purifying mammalian dsRNAases (which could then be further characterized). The dsRNA used in the assay were 17 or 20 nucleotides in length. Crooke considered that purpose to have been fulfilled, as evidenced by the statement, "Having (1) established a reproducible and activity-specific assay for, (2) determined several sources of and (3) achieved an adequate degree of purification of the dsRNases of the invention via the methods described above, the dsRNases are further purified by a variety of means... the assays described herein are used to evaluate the presence or absence of the desired dsRNase in a sample." (col. 52, lines 55-59). There is nothing here to suggest using alternate dsRNA substrates rather than 17 or 20 nt dsRNA substrates in the assay, and certainly nothing to suggest using dsRNAs of 21, 22, or 23 nt rather than 17 or 20 nt. There is nothing to suggest that dsRNA of 21, 22, or 23 nt might differ from 17 or 20 nt dsRNAs with respect to their potential use for purifying and assaying mammalian dsRNAses and no suggestion that the artisan might expect to learn anything new from using slightly longer dsRNA (e.g., 21, 22, or 23 nt) instead of 17 or 20 nt dsRNA for this purpose. Applicant also

respectfully submits that the Examiner has provided no basis for the assertion that, "One of skill would have further recognized that information gleaned from such studies would incidentally have been useful towards the optimization of the RNA gapmer method disclosed therein for targeted degradation of an mRNA via endogenous dsRNase activity, triggered by the introduction of an RNA gapmer" (Office Action, p. 9). There is nothing in Crooke that would lead the skilled artisan to think that studying cleavage of short duplexes might provide any useful information for optimizing the RNA gapmer method for its intended use of causing targeted degradation of a mammalian mRNA. There is nothing in Crooke that would lead the skilled artisan to think that studying cleavage of dsRNA 21, 22, or 23 nucleotides in length might provide any useful information for optimizing the RNA gapmer method for its intended use of causing targeted degradation of a mammalian mRNA beyond the information, if any, that might be gained using dsRNAse substrates 17 or 20 nucleotides long.

If anything, Crooke teaches that efficacy of the gapmers depends at least in part on the specific sequence and/or chemical identity of the nucleosides and internucleoside linkages, and the skilled artisan would have directed his or her attention towards modifying these parameters rather than modifying the length had he or she wanted to optimize the method. Were the Examiner's rationale regarding the desire of the scientist to explore be taken to its logical conclusion, it would in theory render obvious subgenera of oligonucleotides having each and every combination or permutation of nucleosides and internucleoside linkages within the broad genus taught by Crooke (see, e.g., cols. 13 and 14). Applicants respectfully submit that such a conclusion is not supported by the law.

The Reference Does Not Lead The Skilled Artisan To Envision Double Stranded Molecules 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, and 25 Nucleotides In Length

The Examiner contends that the skilled artisan would have, "immediately envisioned chemically and nonchemically modified dsRNAs of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, and 25 nucleotides in length complementary to a mammalian gene". Applicants respectfully disagree and contend that the Examiner's statement is based on hindsight, i.e., the teaching of the instant

invention that dsRNAs of certain lengths are of particular importance in the context of RNAi. Applicants respectfully note that, in addition to teaching size ranges for single-stranded gapmers, Crooke teaches suitable nucleobases and suitable phosphorus linkages, e.g., "suitable nucleobases for incorporation in these nucleoside subunits include purines and pyrimidines such as adenine, guanine, cytosine, uridine, and thymine, as well as other synthetic and natural nucleobases such as xanthine, hypoxanthine, 2-aminoadenine, 6-methyl and other alkyl derivatives of adenine and guanine, 2-propyl and other alkyl derivatives of adenine and guanine, 5-halouracil and cytosine, 5-propynyl uracil and cytosine, 6-azo uracil, cytosine and thymine, 5-uracil (pseudouracil), 4-thiouracil, 8-halo, amino, thiol, thioalkyl, hydroxyl and other 8-substituted adenines and guanines, 5-trifluoromethyl and other 5-substituted uracils and cytosines, 7-methylguanine.". Crooke further teaches that phosphorus linkages include phosphodiester, phosphorothioate, 3'-(or -5')deoxy-3'-(or -5')thio-phosphorothioate, phosphorodithioate, phosphoroselenates, 3'-(or -5')deoxy phosphinates, borano phosphates, 3'-(or -5')deoxy-3'-(or 5'-) amino phosphoramidates, hydrogen phosphonates, borano phosphate esters, phosphoramidates, alkyl or aryl phosphonates and phosphotriester phosphorus linkages. Applicants respectfully submit that collectively the genus of oligonucleotides having these various lengths, nucleobases, and phosphorus linkages contains numerous subgenera and species. Applicants respectfully submit that there is no more reason why, based on Crooke, the skilled artisan would immediately envision a subgenus of oligonucleotides of a particular length than that he or she would envision a subgenus of oligonucleotides having any one or more of the afore-mentioned nucleobases and/or phosphorus linkages, or a combination thereof. Applicants respectfully submit, therefore, that the Examiner's contention that one of skill in the art would immediately envision chemically and nonchemically modified dsRNAs of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, and 25 nucleotides in length complementary to a mammalian gene amounts to a contention that the skilled artisan would immediately envision each subgenus within the genus of oligonucleotides taught by Crooke. Applicants respectfully disagree that such assertion is supported by the law. Instead, Applicants contend that the Examiner has impermissibly used hindsight to construct a set of subgenera based on length while ignoring the full scope of variables (length, nucleobase, phosphorus linkage, etc.) taught by Crooke and has then selected, without any basis in Crooke, particular subgenera 21-23 nucleotides in length out of that set and asserts that Crooke

renders them obvious. Applicants respectfully submit that the Examiner's reasoning, which was clearly guided by the teachings of the instant specification focusing on the ability of dsRNA about 21-23 nucleotides long to mediate RNAi, cannot properly support an obviousness rejection.

In summary, Applicants contend that, even if there were a basis for applying the size range taught for single-stranded RNAs to the context of dsRNAs, which Applicants do not concede, there is no reason other than as disclosed in the instant specification to select a particular narrow subrange (21-23 nucleotides) or any individual length from within such range.

Double Stranded RNA Molecules Of 21, 22, Or 23 Nucleotides In Length Have Surprising Properties

Even assuming arguendo that the Examiner has met his burden of establishing a prima facie case of obviousness with regards to the pending claims of the instant application, the claimed RNAi-mediating molecules have surprising properties which distinguish the instant claims from the prior art. As the Examiner is well aware, an invention that may otherwise appear obvious based upon the prior art may not be so if it produces results that are unexpected in view of such prior art. This secondary consideration which may rebut a *prima facie* case of obviousness allows for the patenting of that which results in a truly surprising and unanticipated benefit or superior property or advantage being conferred upon the public.[1]

The invention is based in part on the surprising discovery that long double-stranded RNA molecules are processed to generate short double-stranded RNA of about 21 to 23 nucleotides. The instant invention is further based on the surprising discovery that dsRNA of about 21 to 23 nucleotides mediates RNAi. As described in the instant specification, dsRNA in the range of about 21 to 23 nucleotides was unexpectedly discovered to achieve RNAi. The discovery that isolated dsRNA of about 21 to 23 nucleotides could mediate RNAi was unexpected because, prior to the instant invention, it had been understood by those skilled in the art that longer segments of dsRNA were the mediators of RNAi (see, e.g., a review regarding the state of art authored by Craig C. Mello, certainly one of the leaders in the RNAi field ... "[I]n most genes, any RNA segment of about 200 to 1000 nucleotides or greater appears to be capable of inducing interference" Science,

[1] In re Soni,54 F.3d 746 (Fed.Cir.1995).

1998 Oct 16;282(5388):430-1)." The discovery that an endogenous cellular process cleaves longer dsRNA into short dsRNA of the claimed size range, as described in the instant specification, led to the recognition that RNAi could be achieved by introducing smaller dsRNA into a cell or organism. The fact that double-stranded RNA in this size range was effective, and also eliminated the problem of interferon induction and cell death that occurred with longer double-stranded molecules, formed the basis for the widespread application of RNAi in mammalian cells and organisms for a variety of purposes.

The Federal Circuit standard for a demonstration of unexpected results of a claimed range is twofold; (1) that the results must be superior and unexpected for the entire claimed range compared to the prior art; and (2) that it is the claimed range itself which is critical to achieving those unexpected results (as opposed to some other confounding factor).[2] In In re Waymouth, the court held that unexpected results for a claimed range as compared with the range disclosed in the prior art had been shown by a demonstration of "a marked improvement, over the results achieved under other ratios, as to be classified as a difference in kind, rather than one of degree."[3] Although the prior art range of possible ratios enveloped the range claimed by appellants, the court found that appellants' evidence demonstrated the necessary unexpected results to overcome an obviousness rejection. Those results followed from the selection of appellants' critical range, which was narrower than the extremely broad inherently disclosed range of the prior art. Additionally in Application of Fushsman, the prior art recited range of 0.1% - 2.0% but the Court found that claims reciting range of 0.1% to 0.7% displayed a strength greater than that of the wider prior disclosed range and contrary to what would be expected from the obvious teaching in the prior art.[4] Thus the rejection based on obviousness was reversed.

Crooke et al. describes various size ranges for single-stranded antisense gapmers, e.g., about 8 to about 50 or about 12 to about 30 *or* about 5 to about 50 or about 15 to about 25. Assuming that these size ranges were to apply to the double-stranded RNA substrates disclosed in Crooke, which

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[2] In re Geisler, 116 F.3d 1465 (Fed.Cir.1997) ("It is not inventive to discover the optimum or workable ranges by routine experimentation." Only if the "results of optimizing a variable" are "unexpectedly good can a patent be obtained for the claimed critical range.").

[3] 499 F.2d 1273, 1276, 182 USPQ 290, 293 (CCPA 1974).

[4] 405 F.2d 892, 852 (C.C.P.A.,1969).

Applicants vehemently deny, the size range claimed by Applicants is tied to the surprising results achieved. In particular, the instant claimed invention is based on the discovery that double-stranded RNAs of about 21-23 nucleotides in length having complementarity to target mRNA mediate RNA interference of such targets, forming the basis for the widespread application of RNAi in mammalian cells and organisms for a variety of purposes. This discovery could in no way have been expected in view of the teaching of dsRNAs of 8 to about 50 or about 12 to about 30 *or* about 5 to about 50 or about 15 to about 25 by Crooke, even if such size ranges were *impliedly* taught for the artificial dsRNA substrates of Crooke, which Applicants do not concede.

Applicant respectfully directs the Examiner's attention to the enclosed Declaration of Dr. P. Zamore, which supports the arguments presented herein regarding the unexpected results discovered by Applicant with respect to the instantly claimed invention.

Thus, the reference fails to provide any guidance for selection of a specific range of sizes of compounds that would be operational in mediating RNA interference. The other cited references do not overcome this deficiency.

Cleavage Products From A Theoretical Digestion Assay Would Not Necessarily Result In Double Stranded RNA Molecules As Presently Claimed

With respect to the Examiner suggestion that if a dsRNA substrate of about 25 to about 50 nucleotides were used in a dsRNA digestion assay taught by Crooke, the resulting cleavage products would "likely be on the order of 10-25 nucleotides in length...Accordingly, one of skill practicing this assay with substrates in the range of 25 to 50-nts in length would necessarily isolate dsRNA cleavage products of between 21 and 23 nucleotides in length." (Office Action, p. 10, lines 1-10), the Applicants would like to make the following remarks of record.

First, as set forth above, the Examiner has failed to provide the requisite motivation to modify the teachings of Crooke to arrive at 25-50 nucleotide ***double-stranded*** RNA substrates or their use in a digestion assay such as that disclosed by Crooke. Second, even if such substrates were made and were cleaved in the assay, isolation of dsRNA cleavage products of between 21 and 23 nucleotides in length would not ***necessarily*** result.

"Inherency...may not be established by probabilities or possibilities. The mere fact that a

certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted)". Applicants respectfully submit that the position at which cleavage occurs and, therefore, the size of resulting cleavage products, depends on the precise structure of the dsRNA substrate. For example, Crooke discloses that cleavage of a duplex formed by a target RNA and single-stranded gapmer occurs within the "gap" region and not within the "wings". In order to conclude that cleavage would result in 21-23 nt cleavage products, it is clear that the "gap" would have to be appropriately positioned within the 25-50 nucleotide dsRNA ***and*** that cleavage would have to occur at the precise position within the gap that would generate 21-23 nucleotide cleavage products. Neither of those is ***necessarily*** the case, even if it were obvious to make double-stranded molecules in this size range and test them, which Applicants deny. Since the fact that a certain result or characteristic ***may*** occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic, it cannot be considered that use of 25-50 nucleotide dsRNA substrates as contemplated by the Examiner would necessarily result in 21-23 nucleotide dsRNA cleavage products.

For all of the foregoing reasons, Applicants respectfully request that the rejection of claims 76-78, 81, 86-88, 91, 108, 110, 112, 115-120 and 124-177 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Crooke et al. (US Patent 6,107,094), as evidenced by Tuschl et al. (US 20040259247 A1) and Amarzguioui et al. (2003) *Nucleic Acids Res.* 31:589-595 be reconsidered and withdrawn.

## Double Patenting Rejection

Claims 76-78, 81, 86-88, 91, 108, 110, 112, 115-120 and 124-177 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 17, 20-23, 76 and 80-85 of copending Application No. 10/255,568. It is requested that the rejection be held in abeyance until allowable subject matter in the cited application is identified. At that time, Applicant will consider filing a terminal disclaimer.

Claims 76-78, 81, 86-88, 91, 108, 110, 112, 115-120 and 124-177 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 30 and 34-55 of copending Application No. 11/142,866. Claims 76-78, 81, 86-88, 91, 108, 110, 112, 115-120, 115-120 and 124-177 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 48, 49, 51, 53-57, 60-64, 67-73 and 75-125 of copending Application No. 10/433,050.

The rejections have been maintained because of a common inventor/assignee. Applicant previously presented arguments that "common ownership" has a specific meaning and refers to a situation when an application has identical ownership. Applicant reiterates all of the arguments previously made of record. Rather than repeating the arguments, it is requested that the Examiner address applicants specific arguments. It is acknowledged that the Examiner has confirmed that the instant application is the earlier filed application. Accordingly, it is requested that this provisional rejection be withdrawn and maintained in the later filed cases if appropriate. However, Applicant respectfully disagree that the double patenting rejection is appropriate as previously discussed.

## CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. W0571.70010US02.

Dated: December 12, 2008

Respectfully submitted,

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